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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/753,752

01/02/2001

Jay M. Short

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02/28/2005

LISA A. HAILE, PH.D.
GRAY CARY WARE & FREIDENRICH LLP
SUITE 1100
4365 Executive Drive
San Diego, CA 92121

EXAMINER

RAMIREZ, DELIA M

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 02/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

44

Advisory Action Before the Filing of an Appeal Brief	Application No. 09/753,752	Applicant(s) SHORT, JAY M.	
	Examiner Delia M. Ramirez	Art Unit 1652	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 31 January 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The reply was filed after the date of filing a Notice of Appeal, but prior to the date of filing an appeal brief. The Notice of Appeal was filed on 31 January 2005. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
- (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ They raise the issue of new matter (see NOTE below);
- (c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☒ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: see attached. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
- The status of the claim(s) is (or will be) as follows:
- Claim(s) allowed: none.
- Claim(s) objected to: none.
- Claim(s) rejected: 1-5.
- Claim(s) withdrawn from consideration: none.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

ADVISORY ACTION

1. Claims 1-5 are pending.
2. The request for entering amendments to the specification, amendment of claims 1, 3, addition of claims 6-7, and arguments filed on 1/31/2005 under 37 CFR 1.116 in reply to the Final Action mailed 7/26/2004 are acknowledged. The proposed amendments to the claims will not be entered. While the amendments to the claims overcome the new matter rejection previously applied to claims 1-5 in regard to “two or more uncultivated organisms”, the instant amendments do not overcome additional grounds of rejections previously applied in regard to 35 USC 112, first paragraph or 103(a), and raise new issues which would require further consideration as discussed below.
3. Proposed amended claim 1 (claims 2 and new claims 6-7 dependent thereof) would be rejected under 35 USC 112, second paragraph due to the recitation of “screening in the liquid phase a library of a mixture of expression clones” for the following reasons. As known in the art, a library of clones is a mixture of different clones, therefore the term “a library of a mixture of expression clones” is unclear and confusing.
4. New claims 6-7 would be rejected under 35 USC 112, second paragraph due to the recitation of “wherein the host cell is” for lacking antecedent basis since there is no host cell recited in claim 1, from which new claims 6-7 depend. For further analysis, these claims will be considered as duplicates of claims 1 or 3.
5. Proposed amended claims 1, 3, claims 2, 4-5 would remain rejected and new claims 6-7 as interpreted would be rejected under 35 USC 112, first paragraph as failing to comply with the written description and enablement requirement.
6. Applicants argue that given the knowledge in the art regarding enzyme activity tests, those of skill in the art could easily determine whether every clone in the library was giving the same positive signal or displaying the same enzymatic characteristic, or whether one or more particular cells were

Art Unit: 1652

producing a positive response that was not common to the whole of the library and hence attributable to the “recovered DNA”. Applicants submit that the subtraction technique does not require use of a host cell whose complete genome is known but can be accomplished simply by ignoring, screening out, or “subtracting out” the enzymatic activities that are commonly produced by the host cells. According to Applicants, this procedure can be done at any temperature or pH to allow discovery of enzymatic activities not produced by the host cells. Applicants also argue that there is no need to know the exact temperature or pH at which the host’s enzyme cease to fully function to practice the claimed invention since one of skill in the art can raise or lower temperature or pH until enzymatic activity common to all of the host cells has been eliminated and only those specific expression products that maintain activity at high temperature or pH are attributable to the “recovered DNA”. It is Applicant’s contention that (1) those of skill in the art of expression libraries can very quickly become familiar with the ranges of pH and temperature tolerance of a host cell found useful for such expression libraries, (2) those of skill in the art would know the pH and temperature optima for a given organisms by looking up that information in the scientific literature or by knowing the conditions of the host’s natural environment, (3) one could conduct a simple test on the host cell alone to determine its ranges of pH and temperature tolerance. In regard to claims 4-5, applicants submit that it would be routine to test for enzymatic activity to discover enzymes having stability under extreme conditions. Thus, Applicants submit that no special skill is required and the invention does not involve highly unpredictable subject matter.

7. Applicant’s arguments are not found persuasive. While it is agreed that testing a library of clones using a known enzymatic activity assay to determine which clones display that activity is well known in the art, it is noted that to determine whether the enzymatic activity detected is attributable to the “recovered DNA”, one of skill in the art need to know whether that activity can also be found in the same host cell used in the library having no exogenous DNA. Since the claims are directed to a method which identifies any enzymatic activity in a library of clones wherein the library is made using any host cell, it is

Art Unit: 1652

unclear as to how one could practice the claimed method if the specification fails to disclose the enzymatic activities which are endogenous to any host cell and the conditions required for those enzymatic activities to be detected such that one could distinguish between enzymatic activity associated with the host cell and that of "recovered DNA". In regard to the argument that the subtraction method does not require knowing the entire genome and all that is required is ignoring, screening out or subtracting out the enzymatic activities commonly produced by the host cells, it is noted that one of skill in the art would have to know which are the enzymatic activities commonly produced by the host cells. It is reiterated herein that the methods claimed require any host cell used in the library, but the specification fails to disclose the enzymatic activities endogenous to any host cell, as encompassed by the claims. Applicant's argument that the exact temperature or pH at which the host's enzymes cease to fully function are not required is not persuasive since as previously indicated if the same enzymatic activity is found in the host cell, in the absence of any knowledge as to pH or temperature conditions associated with the endogenous enzymatic activity, one of skill in the art would not be able to distinguish between endogenous enzymatic activity and that attributable to the "recovered DNA". The Examiner agrees that one could find information in regard to a host cell's growing conditions in scientific literature and one could test different pH and temperature conditions to determine growing conditions for a known organism. However, the claims as written encompass any host cell and any enzymatic activity, known and unknown. Furthermore, pH and temperature conditions which allow cell growth may not be applicable to any enzymatic activity in that host cell. In regard to claims 4-5, it is noted that the claims encompass any enzymatic activity, known and unknown. However, the specification fails to provide an assay to detect any enzymatic activity, pH or temperature ranges for displaying any enzymatic activity, or the substrates associated with any enzyme. Therefore, it is unclear as to how one of skill in the art can reasonably conclude that the claimed invention is adequately described or fully enabled by the teachings of the specification.

Art Unit: 1652

8. Proposed amended claims 1, 3, claims 2, 4-5 would remain rejected and new claims 6-7 as interpreted would be rejected under 35 USC 103(a) as being unpatentable over Yen et al. (US Patent No. 5171684, 1992) in view of More et al. (Appl. Environ. Microbiol. 60(5):1572-1580, 1994). This rejection has been described at length in a previous Office Action mailed on 12/27/2002.

9. Applicants argue that Yen fails to suggest the methods of claims 1 and 3 because Yen fails to disclose any method for screening for enzymes obtained from a mixed population of uncultivated organisms whose DNA was randomly selected for formation of the library. By contrast, it is Applicant's contention that in the Yen's method, the isolated DNA was obtained from a single cultured organism whose enzymatic products were known and its DNA was pretreated. Therefore, Yen fails to suggest creating and screening a DNA library or a library of a mixture of clones that is produced from DNA that is randomly selected from a mixture of uncultivated organisms. According to Applicants, Yen does not suggest mutagenesis of mixed DNA for detection of a specific enzymatic characteristic. In regard to More, Applicants argue that (1) the instant reference teaches that even if the extraction efficiency were improved to 99.9% there would still be a certain amount of cells whose DNA could not be accessed by current methods, and (2) the Examiner asserts that purification of DNA from an SDS treated sediment containing a mixed population of organisms is possible.

10. Applicant's arguments are not found persuasive. It is reiterated herein that the Examiner is not relying on the teachings of Yen et al. in regard to the DNA used in the library. The Examiner acknowledges that Yen et al. teaches the DNA isolated from a single cultured organism. Instead, the Examiner relies on More et al. which teaches isolation of DNA from soil microbial populations. It is noted that while Applicants have amended claims 1 and 3 to recite "DNA randomly selected from uncultivated organisms" or "DNA randomly selected from a mixed DNA population", these limitations are taught by More et al. since no selection process is used by More et al. in regard to the DNA from soil microbial populations which was ultimately isolated. Therefore the DNA was randomly selected. In

Art Unit: 1652

regard to arguments that the DNA extraction taught by More et al. is not complete, it is noted that the claims do not require complete DNA extraction from the uncultivated microorganisms and the specification does not teach complete DNA extraction from uncultivated microorganisms. Furthermore, it is reiterated herein that while it is agreed that More et al. discloses some limitations in regard to the extent of DNA isolation from soil samples, More et al. clearly teach successful DNA isolation from soil samples and how to improve DNA isolation from soil samples (Abstract; page 1579, first column, lines 22-24). Therefore, the teachings of Yen and More combined would render the claimed invention obvious.

11. The rejections previously applied are, therefore, maintained for the reasons of record in view of the non-entry of the proposed amendments.

12. For purposes of Appeal, the status of the claims is as follows:

Claim(s) allowed: NONE

Claims(s) objected to: NONE

Claim(s) rejected: 1-5

Claim(s) withdrawn from consideration: NONE

13. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (571) 273-8300. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

14. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should

Art Unit: 1652

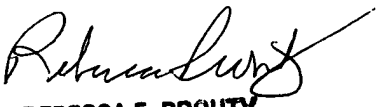
you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
February 24, 2005


REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP 1800
1600